

**AMENDMENTS TO THE SPECIFICATION**

**Please amend paragraph 83 on page 26 as follows:**

Query and individual sequences can be aligned using the methods and computer programs described above, and include BLAST 2.0, available over the world wide web at the world wide website of the NCBI at [ncbi.nlm.nih.gov/BLAST/](http://www.ncbi.nlm.nih.gov/BLAST/)~~http://www.ncbi.nlm.nih.gov/BLAST/~~. See also Altschul, *et al. Nucleic Acids Res.* (1997) 25:3389-3402. Another alignment algorithm is Fasta, available in the Genetics Computing Group (GCG) package, Madison, Wisconsin, USA, a wholly owned subsidiary of Oxford Molecular Group, Inc. Other techniques for alignment are described in Doolittle, *supra*. Preferably, an alignment program that permits gaps in the sequence is utilized to align the sequences. The Smith-Waterman is one type of algorithm that permits gaps in sequence alignments. See *Meth. Mol. Biol.* (1997) 70: 173-187. Also, the GAP program using the Needleman and Wunsch alignment method can be utilized to align sequences.

**Please amend paragraph 95 on page 30 as follows:**

Profiles can be designed manually by (1) creating an MSA, which is an alignment of the amino acid sequence of members that belong to the family and (2) constructing a statistical representation of the alignment. Such methods are described, for example, in Birney *et al.*, *Nucl. Acid Res.* (1996) 24(14):2730-2739. MSAs of some protein families and motifs are publicly available. For example, <http://genome.wustl.edu/Pfam/> includes MSAs of 547 different families and motifs. These MSAs are described also in Sonnhammer *et al.*, *Proteins* (1997) 28: 405-420. Other sources over the world wide web include the world wide web site of EMBL at [embl-heidelberg.de/argos/ali/ali.html](http://embl-heidelberg.de/argos/ali/ali.html) ~~at <http://www.embl-heidelberg.de/argos/ali/ali.html>~~; alternatively, a message can be sent to [ALI@EMBL-HEIDELBERG.DE](mailto:ALI@EMBL-HEIDELBERG.DE) for the information. A brief description of these MSAs is reported in Pascarella *et al.*, *Prot. Eng.* (1996) 9(3):249-251. Techniques for building s from MSAs are described in Sonnhammer *et al.*, *supra*; Birney *et al.*, *supra*; and "Computer Methods for Macromolecular Sequence Analysis," *Methods in Enzymology* (1996) 266, Doolittle, Academic Press, Inc., San Diego, California, USA.

**Please amend paragraph 136 starting on page 44 as follows:**

Mapping. Polynucleotides of the present invention can be used to identify a chromosome on which the corresponding gene resides. Such mapping can be useful in identifying the function of the polynucleotide-related gene by its proximity to other genes with known function. Function can also be assigned to the polynucleotide-related gene when particular syndromes or diseases map to the same chromosome. For example, use of polynucleotide probes in identification and quantification of nucleic acid sequence aberrations is described in USPN 5,783,387. An exemplary mapping method is fluorescence in situ hybridization (FISH), which facilitates comparative genomic hybridization to allow total genome assessment of changes in relative copy number of DNA sequences (see, *e.g.*, Valdes *et al.*, *Methods in Molecular Biology* (1997) 68:1). Polynucleotides can also be mapped to particular chromosomes using, for example, radiation hybrids or chromosome-specific hybrid panels. See Leach *et al.*, *Advances in Genetics*, (1995) 33:63-99; Walter *et al.*, *Nature Genetics* (1994) 7:22; Walter and Goodfellow, *Trends in Genetics* (1992) 9:352. Panels for radiation hybrid mapping are available from Research Genetics, Inc., Huntsville, Alabama, USA. Databases for markers using various panels are available via the world wide web at the world wide website of SHGC at [shgc-www.stanford.edu](http://shgc-www.stanford.edu) <http://F/shgc-www.stanford.edu>; and at the world wide website of the Whitehead Institute/MIT Center for Genome Research at [genome.wi.mit.edu/cgi-bin/contig/rhmapper](http://genome.wi.mit.edu/cgi-bin/contig/rhmapper), <http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>. The statistical program RHMAP can be used to construct a map based on the data from radiation hybridization with a measure of the relative likelihood of one order versus another. RHMAP is available *via* the world wide web of SPH at [sph.umich.edu/group/statgen/software](http://www.sph.umich.edu/group/statgen/software) <http://www.sph.umich.edu/group/statgen/software>. In addition, commercial programs are available for identifying regions of chromosomes commonly associated with disease, such as cancer.

**Please amend paragraph 229 starting on page 78 as follows:**

Each of the profile hits is described in more detail below. Table 4 provides the corresponding SEQ ID NO of the provided polynucleotides that encode gene products with similarity or identity to the profile sequences. Similarity (strong or weak) is also noted in Table 4. The acronyms for the profiles

(provided in parentheses) are those used to identify the profile in the Pfam and Prosite databases. The Pfam database can be accessed through any of the following URLs: wustl.edu/index, sanger.ac.uk/Software/Pfam/, and cgr.ki.se/Pfam/ ~~http://pfam.wustl.edu/index.html;~~ ~~http://www.sanger.ac.uk/Software/Pfam/;~~ and ~~http://www.cgr.ki.se/Pfam/~~. The Prosite database can be accessed at the expasy website at expasy.ch/prosite/ ~~http://www.expasy.ch/prosite/~~. The public information available on the Pfam and Prosite databases regarding the various profiles, including but not limited to the activities, function, and consensus sequences of various proteinss families and protein domains, is incorporated herein by reference.

**Please amend paragraph 233 on page 80 as follows:**

Seven Transmembrane Integral Membrane Proteins -- Rhodopsin Family (7tm 1; Pfam Accession No. PF00001). SEQ ID NO:3 corresponds to a gene encoding a polypeptide that is a member of the seven transmembrane (7tm) receptor rhodopsin family. G-protein coupled receptors of the (7tm) rhodopsin family (also called R7G) are an extensive group of hormones, neurotransmitters, and light receptors which transduce extracellular signals by interaction with guanine nucleotide-binding (G) proteins (Strosberg A.D. *Eur. J. Biochem.* (1991) 196:1, Kerlavage A.R. *Curr. Opin. Struct. Biol.* (1991) 1:394, Probst, et al., *DNA Cell Biol.* (1992) 11:1, Savarese, et al., *Biochem. J.* (1992) 283:1, or the following URLs: gcrdb.uthscsa.edu and swift.embl- ehidelberg.de/7tm/ ~~http://www.gcrdb.uthscsa.edu/;~~ ~~http://swift.embl-heidelberg.de/7tm/~~. The consensus pattern that contains the conserved triplet and that also spans the major part of the third transmembrane helix is used to detect this widespread family of proteins: [GSTALIVMFYWC]-[GSTANCPDE]-{EDPKRH}-x(2)-[LIVMNQGA]-x(2)-[LIVMFT]-[GSTANC]-[LIVMFYWSTAC]-[DENH]-R-[FYWCSH]-x(2)-[LIVM].